

Systematic Review and Evidence Based Guidance on the Surgical Antibiotic Guidelines Adherence

Hani Helal Khader Alhassani ,Khalid Mohamad Gormallh Al-Ghamdi ,Ahmad Hameed Allehaiby ,Moataz Abdulhalim Mohammed, Maram Adnan Rawah ,Saleh Jamaan Alzahrani, Alyaa Mohammed Raffie A Banjar ,Sarah Musaed Alluheibi ,Abdullah Mohammed Sindi ,Hassan Omar Qahwaji ,Sara Abdo Saif ,Raghad Abdulrahman Rasheed ,Ali Hussein Mohammed Alasmri ,Badr Fouad Mogharbel ,Sulafah Sameer Abduljawad ,Rayan Tareq Jameel Alrefai, Sultana Sameer Saeedi
Faculty of general surgery, King Abdulaziz hospital, Jeddah, Saudi Arabia

ABSTRACT

Background: antibiotic administration is an essential element for any surgical operation success, even if a prior infection was not detected. This is due to the fact that antimicrobial agents do not only act as therapy to treat preexisting infection but also as a prophylaxis which is given preoperatively to reduce the incidence of surgical site infection and as an adjunct to operative treatment which is given in the setting of operative management of infections such as secondary peritonitis or necrotizing fasciitis. Prophylactic antibiotics are also used as primary therapy when operation is not performed, such as for cellulitis, or postoperative pneumonia which indicates the significance of surgical antibiotic prophylaxis and the great importance of adhering to the right treatment protocol and guidelines.

Aim of the Study: a systematic review was performed to evaluate the adherence to clinical guidelines for surgical antibiotic prophylaxis. **Methods:** of which fifteen studies were retrieved that fulfilled most of the inclusion requirements of being randomized controlled clinical trials.

Results: 952 articles were retrieved from database, of which 15 studies were selected for selected for synthesis. 5 outcome of interest were identified, on top of which were the administration of antibiotic at the correct time and adequate discontinuation of antibiotic which ranged from 0.3% to 100%.

Conclusion: the assessed studies addressed a gap in the adherence to guidelines for surgical antibiotic prophylaxis and more rigor approaches to leverage the guidelines.

Keywords: Surgical site infection, SSI, Prophylaxis, Antibiotic, Systematic review, Guideline adherence.

INTRODUCTION

Surgical site infections (SSIs) are a common cause of healthcare-associated infection. The United States Centers for Disease Control and Prevention (CDC) has developed criteria that define surgical site infection as infection related to an operative procedure that occurs at or near the surgical incision within 30 or 90 days of the procedure, depending on the type of procedure performed⁽¹⁾. SSIs are often localized to the incision site but can also extend into deeper adjacent structures.

SSIs are the most common and costliest healthcare-associated infections^(3,4). Among surgical patients, SSIs account for 38 percent of nosocomial infections. It is estimated that SSIs develop in 2 to 5 percent of the more than 30 million patients undergoing surgical procedures each year (i.e., 1 in 24 patients who undergo inpatient surgery in the United States has a postoperative SSI)^(5,6).

Antibiotic prophylaxis is aimed to reduce the incidence of SSI by preventing the development of infection caused by organisms that colonize or contaminate the surgical site. The main target of antibiotic prophylaxis is the wound. Antibiotics are administered to the patient to reduce the bacterial load, so that it

does not overwhelm the host natural defenses, causing infection⁽⁷⁾. The adequate use of perioperative antibiotic prophylaxis can reduce the rate of SSI in up to 50%⁽⁸⁾.

Efforts have been undertaken to establish guidelines for the appropriate use of antibiotic prophylaxis. These guidelines are designed to provide professionals with a standardized approach to rational, safe and effective use of antimicrobial agents for the prevention of SSI, and their content is based on current available clinical evidence, besides emerging issues⁽⁹⁾.

Although the principles of antimicrobial prophylaxis in surgery are clearly established and several guidelines have been published, the implementation of these guidelines has been impaired by multiple factors⁽¹⁰⁾. Some possible reasons include the difficulty encountered by professionals to update their knowledge, their dependence on habits originated in clinical practice rather than in evidence, the lack of policies, and failures in the implementation of norms and institutional guidelines⁽¹¹⁾.

In view of the aforementioned, the present review aimed to assess the adherence to guidelines for surgical antibiotic prophylaxis,

by analyzing studies on the application of local, national and/or international guidelines.

METHODS

The review included the articles published from July 2004 to July 2014, based on the following databases: Medline (via PubMed), the search strategies were designed according to the specificity of each database, considering three main research indexes: title, abstract, and topic. The following representation of subject and free text terms was observed: Antibiotic prophylaxis, prophylactic antibiotic, antimicrobial prophylaxis, prophylaxis, surgery, surgical patient, surgical wound infection, postoperative wound infection, surgical procedure, operative, operative surgical procedure, guideline adherence, evaluation, adherence, surveillance, appropriate, appropriateness.

Inclusion criteria for selection of articles

1. Population: studies in patients aged 18 or over;
2. Articles portraying themes related to adherence to guidelines for surgical antibiotic prophylaxis
3. Studies on surgical procedures on the following specialties: gynecology, urology, vascular surgery, otorhinolaryngology, neurosurgery, thoracic surgery, general surgery, plastic surgery.

Exclusion criteria for selection of articles

1. Articles whose main purpose was to correlate antibiotic prophylaxis to the occurrence of SSI;
2. Articles exclusively or mostly on:
3. Pediatric patients
4. Emergency procedures and/or trauma
5. Endoscopic exams
6. Surgical procedures of the following specialties: cardiac surgery, orthopedics, odontology, oral and maxillofacial surgery, dermatology, ophthalmology and obstetrics.

The outcomes assessed in the 18 selected studies were as follows: (1) appropriate indication of antibiotic prophylaxis; (2) inappropriate indication of antibiotic prophylaxis; (3) antibiotic administration at the correct time; (4) correct antibiotic choice; (5) adequate discontinuation of antibiotic; and (6) adequate antibiotic prophylaxis.

The outcomes of interest analyzed in the articles were considered appropriate or not, according to the observance of predefined parameters of antibiotic prophylaxis protocols/guidelines adopted in each article. The antibiotic prophylaxis was considered adequate when there was adherence to the

criteria established in the guidelines adopted in each study.

Each article was assessed by two independent reviewers and all data were extracted by these reviewers. Details on population, themes, type of surgical procedures, appropriate indication of antibiotic prophylaxis, inappropriate indication, antibiotic administration at the correct time, correct antibiotic choice, adequate discontinuation of antibiotic, and adequate antibiotic prophylaxis were independently extracted. A third reviewer was consulted in the event of a disagreement.

The present study was in line with a systematic review with the purpose performed by Marise Gouvêa et al. ⁽¹²⁾

RESULTS

The search recovered 952, and 35 articles were found to be duplicates. After assessment of the titles and abstracts of the 821 articles were identified, 796 articles were excluded because they included unrelated or unsuitable subjects. Of the 25 articles eligible for analysis, 11 full-text articles were excluded.

One article obtained by manual search was added to the remaining full 14 articles, totaling 15 studies that were included in the synthesis.

The present study has included 15 studies in the synthesis, 9 were conducted in Europe, 3 in Asia, 1 in Oceania and 2 in America.

General characteristics of the assessed studies : (Table 1)

Study Design ⁽¹²⁾

- There were 8 cross-sectional studies, 6 prospective cohort and 2 retrospective cohort)
- Levels of evidence ranging from IV to VI.8
- The sample sizes ranged between 84 and 545,322 individuals.
- Surgical specialties contemplated, the studies involved General surgery (2 studies), Otorhinolaryngology (1), Gynecology (2), Urology (1), and (9) studies involved multiple specialties (General surgery, Cardiac surgery, Neurosurgery, Gynecology-obstetrics, Ophthalmology, Orthopedics, Otorhinolaryngology, Urology, Vascular, Plastic, Thoracic and Oral and maxillofacial surgery).
- Significant variations were observed in all assessed outcomes of interest, as described in **Table 2**.
- Consolidated Outcome is explained in **Table 3**.

Table 1: General characteristics of the assessed studies.

Author/year/place	Sample	Study design	Level of evidence
(Gul et al.,2005) Malaysia	419	Cross-sectional	VI
(Askarian et al.,2006) Iran	1000	Prospective cohort	IV
(Castella et al.,2006) Italy	803	Cross-sectional	VI
(Bull et al.,2006) Australia	10,643	Retrospective cohort	IV
(Fennessy et al.,2006) Ireland	131	Prospective cohort	IV
(Malavaud et al.,2008a) France	84	Cross-sectional	VI
(Tourmousoglou et al.,2008) Greece	890	Prospective cohort	IV
(Malavaud et al.,2008b) France	100	Cross-sectional	VI
(Mahdaviazad,2011) Iran	365	Cross-sectional	VI
(Meeks et al.,2011) United States	517	Retrospective cohort	IV
(Durando et al.,2012) Italy	717	Prospective cohort	IV
(Hohmann et al.,2012) Germany	5064	Prospective cohort	IV
(Machado-Alba et al.,2013) Colombia	211	Cross-sectional	VI
(Napolitano et al.,2013) Italy	382	Cross-sectional	VI
(Pittalis et al.,2013) Italy	2835	Prospective cohort	IV

Table 2 : shows significant results variation among the 15 assessed studies.

	Appropriate indication	Inappropriate indication	Administration at the correct time	Correct choice	Appropriate discontinuation	Appropriate antibiotic prophylaxis
No. of Studies	4	5	13	10	9	12
% Prevalence adequate indication	70.3% to 95%	5% to 100%	39.7% to 100%	22% to 95%	5.8% to 91.4%	0.3% to 84.5%
N	N= 717 and 2835	N = 2835 and 322	N = 100 and 890	N = 97 And 803	N = 1000 and 100	N = 1000 and 2835
Surgical specialties addressed	Urology , General Surgery ,Gynecology and multiple specialties	General Surgery , Gynecology and multiple specialties	General Surgery , Otorhinolaryngology Urology and multiple specialties	Urology ,General Surgery and multiple specialties	General Surgery and multiple specialties	Urology , General Surgery ,Gynecology and multiple specialties

Table 3: Consolidated outcome for the significant variations observed in all assessed studies.

Author/year /place	Appropriate indication	Inappropriate indication	Administration at the correct time	Correct AB choice	Appropriate discontinuation	Appropriate antibiotic prophylaxis
(Gul et al., 2005) Malaysia	ND	ND	98%	87% ^A 22% ^B 84.3% ^C	20% ^A 48% ^B 69% ^C	ND
(Askarian et al., 2006) Iran	ND	98%	ND	ND	5.80%	0.30%
(Castella et al., 2006) Italy	ND	ND	84%	95%	80%	ND
(Bull et al., 2006) Australia	ND	ND	76.40%	53.30%	ND	81.10%
(Fennessy et al., 2006) Ireland	ND	5% ^D , 30% ^E , 66% ^F , 80% ^G , 96% ^H , 100% ^A	40%	ND	ND	ND
(Malavaud et al., 2008a) France	88.10%	ND	72.90%	91.90%	ND	58.30%
(Tourmousoglou et al., 2008) Greece	ND	19%	100%	70%	36.30%	36.30%
(Malavaud et al., 2008b) France	85%	ND	39.70%	82.80%	91.40%	42%
(Mahdaviiazad, 2011) Iran	ND	64.60%	61.10%	25.40%	29.40%	10.13%
(Meeks et al., 2011) U.S.	ND	ND	79%	65%	82%	62%
(Durando et al., 2012) Italy	70.30%	ND	75.70%	ND	ND	35.50%
(Hohmann et al., 2012) Germany	ND	ND	ND	ND	67.10%	70.70%
(Machado-Alba et al., 2013) Colombia	ND	ND	45.50%	ND	ND	44.50%
(Napolitano et al., 2013) Italy	ND	ND	53.40%	25.50%	ND	18.10%
(Pittalis et al., 2013) Italy	95%	5%	50%	84.50%	48%	84.50%

Outcomes analysis

- Appropriate indication of antibiotic prophylaxis.
- Inappropriate indication of antibiotic prophylaxis.
- Antibiotic administration at the correct time.
- Correct antibiotic choice.
- Appropriate discontinuation of antibiotic prophylaxis.
- Adequate antibiotic prophylaxis = adherence to the protocols of antibiotic prophylaxis adopted.

ND = not described.

Considered appropriate/inappropriate, correct and adequate when the predefined parameters of antibiotic prophylaxis protocols adopted in each article are observed.

Surgeries – ^A: colorectal, ^B

DISCUSSION

The preliminary step in judicious antibiotic administration is to understand what can be expected from their use. SSI development is multifactorial, one factor would be the amount and nature (virulence) of bacterial contamination, other factors would be local conditions (wound), and susceptibility and immunity of the host (patient). Thus, prevention of SSI must be seen as a chain of factors, including patient condition, surgical preparation, antimicrobial administration strategy, potential for contamination in the surgical environment, and wound condition (depends on the quality of surgical technique). The strength of this chain is limited by its weakest link. Increasing the antibiotics administered (i.e., type, dose, duration) to patients involved in excessively traumatic surgical procedures or when poor aseptic technique has been used will not necessarily lower the SSI rates but can favor bacterial resistance and clinical adverse effects. Similarly, using antibiotics locally within the peritoneal and thoracic cavities is not recommended, as these agents induce local inflammation and have not proven beneficial.

Hence, The selection and duration of antibiotic prophylaxis should cause the least possible impact on the patient microbiota⁽¹³⁾. Therefore, it is extremely important to observe the guidelines for administration of a correct antibiotic prophylaxis.

Although guidelines are revised regularly, it is observed that there is a lack of awareness of these revised versions by doctors. It is a challenge to disseminate evidence-based knowledge systematically into clinical practice⁽¹⁰⁾.

In the present study, we intended to shed more light on the importance of adherence to the standard guidelines, since following “own” guidelines may not only deprive patients from the right to optimize their recovery rate and convenience but also result into excessive complications, malpractice insurance costs, managed care systems⁽¹⁴⁾ and excessive workload for the practitioners and worse, when the infection outbreak happens after the discharge of the patient, another surgeon/doctor might receive the patient which can make the treatment and healthcare harder for both.

The busy practitioner who seeks an excuse for the difficulty he or she faces in keeping up to date with evidence-based medicine should rely

on formal clinical guidelines as an acceptable means of adopting safe clinical practice. This will hopefully reduce the haphazard abuse of antibiotic administration and its undesirable consequences⁽¹¹⁾.

Because of the diversity of guidelines adopted in the different studies, it has been difficult to compare adherence to guidelines regarding the outcomes of interest in the present review. The comparisons of results between the studies should be made with caution, as the discrepancies can be partly attributed to factors such as: populations of different studies, studies conducted in different countries, comparison of studies on a single type of surgical procedure or between very different surgical specialties, different methods used in the studies, different guidelines of antibiotic prophylaxis adopted (including in the same study), partial analysis of outcomes of interest in some studies (only in the cases where the administration of antibiotics was appropriately indicated), and the possibility of incomplete records in patient charts. Levy *et al.*,⁽¹⁵⁾ in their report, have already observed that the internal validity (methodological rigor) and external validity (generalizability) of studies on surgical antibiotic prophylaxis are poor and even the results may be context-sensitive.

The outcome adequate antibiotic prophylaxis was the second outcome most described in the reviewed studies, with 13 studies addressing this parameter. Antibiotic prophylaxis was considered adequate when there was adherence to the criteria established in the guidelines adopted in each study. Even when adherence to guideline was 84% in one of the studies, antibiotic prophylaxis was considered inadequate in all the studies, which is consistent with Bratzler⁽¹⁶⁾ who states that, although the administration of chemoprophylaxis in surgery is well-accepted and standardized, surgeons not always adhere to the existing guidelines. According to the same author, given the wide range of evidence-based recommendations, appropriate antimicrobial prophylaxis should be a practice relatively easy to implement. However, many patients are still undergoing surgeries without a satisfactory antibiotic prophylaxis.

Of all the outcomes defined for analysis in this review, the one that was least addressed by the selected studies was appropriateness of indication of antibiotic prophylaxis, which was

addressed in five studies only. Despite the prevalence of more than 70.3% of the studies, and of the lower variability in the results when the studies were compared, in none of them appropriate indication of antibiotic prophylaxis was satisfactory. The second outcome less evaluated in the studies was inappropriate indication of antibiotic prophylaxis and it showed the highest variability among studies. The results obtained for the two above-mentioned outcomes demonstrate that the practices adopted do not observe the recommendations made by Tavares⁽¹⁷⁾ who reports that the prophylactic use of antimicrobials in surgery is justified if there is high risk of surgical wound infection, or if this infection may generate severe consequences. The McDonnell Norms Group⁽¹⁸⁾ addresses adverse consequences such as direct toxicity, change in the normal microbiota, and promotion of bacterial resistance, when antibiotics are inappropriately prescribed.

The nine studies where appropriate discontinuation of antibiotic was described also showed a significant variation, ranging from 5.8% to 91.4%. The adherence of the studies with this outcome was not considered satisfactory and is not consistent with authors that claim that a more prolonged administration of prophylactic antibiotics did not favor the prevention of surgical wound infection, and may encourage the development of microbial resistance, in addition to being costly to patients, increasing the direct costs of care^(19,20).

Of the 18 studies reviewed, 10 described the correct antibiotic choice, and also showed discrepant results, with values ranging from 22% to 95% and poor adherence to the guidelines. Bratzler *et al.*⁽⁹⁾ claim that the antimicrobial agent selected must be active against the most common pathogens that occur in the surgical site, considering the safety profile and patient allergy to certain antibiotics. It is desirable that the antibiotic chosen be cheap, of low toxicity and with a half-life sufficiently prolonged to maintain adequate concentration until the wound has been closed⁽¹⁹⁾.

Most studies selected analyzed the outcome administration of antibiotic at the correct time. Out of the 14 studies included, only one showed 100% adherence to the adopted guideline, while the remaining 13 did not show adequate results, in disagreement with the current regulations. According to Bratzler,⁽¹³⁾ antibiotic prophylaxis aims to achieve blood and tissue levels of the

drug that exceed the minimum inhibitory concentration (MIC) for the microorganisms likely to be encountered. Therefore, antibiotics should be administered at the correct time. The success of antimicrobial prophylaxis requires the availability of the drug at the surgical site before contamination occurs⁽⁹⁾. It is important to stress that the moment considered appropriate for antibiotic administration varied between the guidelines adopted in the studies reviewed.

After analysis of the studies selected for this review, the great variability of methods used in the study of the subject, and in most cases the design of the study generated low levels of evidence (IV and VI), with the absence of randomized clinical trials on the theme.

Antibiotics cannot be indiscriminately administered to any surgical patient in order to prevent postoperative infections. Such use is not only unnecessary in many surgical situations but it also makes the treatment more expensive and contributes to the selection of resistant organisms. In addition, it can be harmful, due to the side-effects of antibiotics. It is up to the medical professionals involved to observe the essential principles of asepsis and antisepsis, recommending the prophylactic use of antibiotics for the surgery, choose the adequate drug, administer at the correct time and discontinue antibiotic prophylaxis at the appropriate time⁽¹⁷⁾. According to Salkind,⁽²⁰⁾ the professionals that give support to surgical procedures have the opportunity to interfere in order to reduce the incidence of SSI when they understand which surgeries require the administration of prophylactic antibiotics, which antibiotic is appropriate, and when it should be administered and discontinued.

Finally, we observed that all the studies reviewed concluded that greater adherence to the guidelines for surgical antibiotic prophylaxis is required. It is clearly necessary that hospital managers and doctors become involved in initiatives aimed to the application of guidelines.⁽²¹⁾ Therefore, surgeons and anesthesiologists, the professionals who decisively contribute to the reduction of postsurgical infectious complications of patients, are essential in this scenario.

CONCLUSION

Despite the fact that the study was observed in all the outcomes assessed, and all the studies indicated a need for greater adherence to guidelines for surgical antibiotic prophylaxis.

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